

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Ellis Reinherz, Linda Clayton, Timothy D. Ocain and Raymond J. Patch  
Application No.: 08/948,124 Group Art Unit: 1816  
Filed: October 9, 1997  
Title: THYMOCYTE CASPASE ACTIVITY AND NEGATIVE SELECTION

CERTIFICATE OF MAILING	
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231	
on 6/10/98	<i>Marlene R. Fitch</i>
Date	Signature
Marlene R. Fitch	
Typed or printed name of person signing certificate	

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

This Information Disclosure Statement is submitted:

- ☐ under 37 CFR 1.129(a), or  
(First/Second submission after Final Rejection)
- ☒ under 37 CFR 1.97(b), or  
(Within three months of filing national application; or date of entry of the national stage in international application; or before mailing date of first office action on the merits; whichever occurs last)
- ☐ under 37 CFR 1.97(c) together with either:
- ☐ a Statement under 37 CFR 1.97(e), as checked below, or
- ☐ a \$240.00 fee under 37 CFR 1.17(p), or  
(After the 37 CFR 1.97(b) time period, but before final action or notice of allowance, whichever occurs first)
- ☐ under 37 CFR 1.97(d) together with:
- ☐ a Statement under 37 CFR 1.97(e), as checked below, and
- ☐ a Petition under 37 CFR 1.97(d)(2), and
- ☐ a \$130.00 petition fee set forth in 37 CFR 1.17(l).  
(Filed after final action or notice of allowance, whichever occurs first, but before payment of the issue fee)
- ☐ Applicant requests that the attached IDS and cited reference(s) \_\_\_\_\_ be placed in the application filewrapper.  
(Filed after payment of issue fee)

Statement Under 37 CFR 1.97(e)

- ☐ Each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement; or
- ☐ No item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the undersigned, after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

Enclosed herewith is form PTO-1449:

- ☒ Copies of the cited references (AL, AR-AZ, AR2-AZ2, AR3-AZ3, AR4-AZ4 and AR5-AV5) are enclosed.
- ☐ Copies of cited references are enclosed except those entered in prior application, U.S. Serial No. \_\_\_\_\_, and references that are not required to be submitted under 37 CFR 1.98.
- ☐ The listed references were cited in the enclosed International Search Report in a counterpart foreign application.

Concise Explanation Requirement (non-English references):

- ☐ The "concise explanation" requirement for reference(s) \_\_\_\_\_ under 37 CFR 1.98(a)(3) is satisfied by:
- ☐ the explanation provided on the attached sheet.
- ☐ the explanation provided in the Specification.
- ☐ submission of the enclosed International Search Report.
- ☐ the enclosed English language abstract.

It is requested that the information disclosed herein be made of record in this application.

Method of payment:

- ☐ Enclosed is a check in the amount of \$ \_\_\_\_\_.
- ☐ Please charge Deposit Account 08-0380 in the amount of \$ \_\_\_\_\_.
- ☐ A copy of this Statement is enclosed.
- ☒ Please charge any deficiency in fees and credit any overpayment to Deposit Account 08-0380.

Respectfully submitted,

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Dated: June 9, 1998

FORM PTO-1449

(REV. 7-80)

INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION

(Use several sheets if necessary)

ATTY. DOCKET NO.

DFCI-522A

SERIAL NO.

08/948,124

APPLICANT

Ellis Reinherz, et al.

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GROUP

1816

## U.S. PATENT DOCUMENTS

EXAM- INER INI- TIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB- CLASS	FILING DATE IF APPROPRIATE
	AA						
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB- CLASS	TRANSLATION YES NO
	AL	WO 97/10711	27 Mar 97	PCT			
	AM						
	AN						
	AO						
	AP						
	AQ						

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	AR	Fowlkes and Pardoll, "Molecular and Cellular Events of T Cell Development", Adv. Immunol., 44:207-264 (1989)
	AS	Nossal, "Negative Selection of Lymphocytes", Cell, 76:229-239 (1994)
	AT	Murphy et al., "Induction by Antigen Of Intrathymic Apoptosis of CD4 <sup>+</sup> CD8 <sup>+</sup> TCR <sup>lo</sup> Thymocytes in Vivo", Science, 250:1720-1723 (1990)

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AU	Trauth et al., "Monoclonal Antibody-Mediated Tumor Regression by Induction of Apoptosis", <i>Science</i> , 245:301-305 (1989)		
AV	Yonehara et al., "A Cell-Killing Monoclonal Antibody (ANTI-Fas) to a Cell Surface Antigen Co-Downregulated with the Receptor of Tumor Necrosis Factor", <i>J. Exp. Med.</i> , 169:1747-1756 (1989)		
AW	Itoh and Nagata, "A Novel Protein Domain Required for Apoptosis", <i>J. Biol. Chem.</i> , 268(15):10932-10937 (1993)		
AX	Alderson et al., "Regulation of Apoptosis and T Cell Activation by Fas-Specific mAb", <i>Intl. Immunol.</i> , 6(11):1799-1806 (1994)		
AY	Takahashi et al., "Generalized Lymphoproliferative Disease in Mice, Caused by a Point Mutation in the Fas Ligand", <i>Cell</i> , 76:969-976 (1994)		
AZ	Tartaglia et al., "A Novel Domain Within the 55 kd TNF Receptor Signals Cell Death", <i>Cell</i> , 74:845-853 (1993)		
AR2	Chinnaiyan et al., "Signal Transduction by DR3, a Death Domain-Containing Receptor Related to TNFR-1 and CD95", <i>Science</i> , 274:990-992 (1996)		
AS2	Yang and Korsmeyer, "Molecular Thanatopsis: A Discourse on the BCL2 Family and Cell Death", <i>Blood</i> , 88(2):386-401 (1996)		
AT2	Nalin, "Apoptosis Research Enters the ICE Age", <i>Structure</i> , 3:143-145 (1995)		
AU2	Henkart, "ICE Family Proteases: Mediators of All Apoptotic Cell Death?", <i>Immunity</i> , 4:195-201 (1996)		
AV2	Alnemri et al., "Human ICE/CED-3 Protease Nomenclature", <i>Cell</i> , 87:171 (1996)		
AW2	Muzio et al., "FLICE, A Novel FADD-Homologous ICE/CED-3-Like Protease, Is Recruited to the CD95 (Fas/APO-1) Death-Inducing Signaling Complex", <i>Cell</i> , 85:817-827 (1996)		
AX2	Duan et al., "ICE-LAP6, a Novel Member of the ICE/Ced-3 Gene Family, Is Activated by the Cytotoxic T Cell Protease Granzyme B", <i>J. Biol. Chem.</i> , 271(28):16720-16724 (1996)		
AY2	Fernandes-Alnemri et al., "In vitro Activation of CPP32 and Mch3 by Mch4, a Novel Human Apoptotic Cysteine Protease Containing Two FADD-Like Domains", <i>Proc. Natl. Acad. Sci. USA</i> , 93:7464-7469 (1996)		
AZ2	Chinnaiyan et al., "FADD/MORT1 Is a Common Mediator of CD95 (Fas/APO-1) and Tumor Necrosis Factor Receptor-Induced Apoptosis", <i>J. Biol. Chem.</i> , 271(9):4961-4965 (1996)		
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## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

AR3	Duan et al., "ICE-LAP3, a Novel Mammalian Homologue of the <i>Caenorhabditis elegans</i> Cell Death Protein Ced-3 Is Activated During Fas- and Tumor Necrosis Factor-Induced Apoptosis", <i>J. Biol. Chem.</i> , 271(3):1621-1625 (1996)
AS3	Schlegel et al., "CPP32/Apopain Is a Key Interleukin 1 $\beta$ Converting Enzyme-like Protease Involved in Fas-mediated Apoptosis", <i>J. Biol. Chem.</i> , 271(4):1841-1844 (1996)
AT3	Chapman, K.T., "Synthesis of a Potent Reversible Inhibitor of Interleukin-1 $\beta$ Converting Enzyme", <i>Bioorg. Med. Chem. Lett.</i> , 2:613-618 (1992)
AU3	Thornberry et al., "A Novel Heterodimeric Cysteine Protease is Required for Interleukin-1 $\beta$ Processing in Monocytes", <i>Nature</i> , 356:768-774 (1992)
AV3	Thornberry et al., "Inactivation of Interleukin-1 $\beta$ Converting Enzyme by Peptide (Acyloxy)methyl Ketones", <i>Biochemistry</i> , 33:3934-3940 (1994)
AW3	Rotonda et al., "The Three-Dimensional Structure of Apopain/CPP32, a Key Mediator of Apoptosis", <i>Nature Struct. Biol.</i> , 3(7):619-625 (1996)
AX3	Pronk et al., "Requirement of an ICE-Like Protease for Induction of Apoptosis and Ceramide Generation by REAPER", <i>Science</i> , 271:808-810 (1996)
AY3	Fearnhead et al., "An Interleukin-1 $\beta$ -Converting Enzyme-like Protease is a Common Mediator of Apoptosis in Thymocytes", <i>FEBS Lett.</i> , 375:283-288 (1995)
AZ3	Ramarli et al., "Selective Inhibition of Interleukin 2 Gene Function Following Thymocyte Antigen/Major Histocompatibility Complex Receptor Crosslinking: Possible Thymic Selection Mechanism", <i>Proc. Natl. Acad. Sci. USA</i> , 84:8598-8602 (1987)
AR4	Kappler et al., "T Cell Tolerance by Clonal Elimination in the Thymus", <i>Cell</i> , 49:273-280 (1987)
AS4	Vasquez et al., "In Vivo and In Vitro Clonal Deletion of Double-Positive Thymocytes", <i>J. Exp. Med.</i> , 175:1307-1316 (1992)
AT4	Ashton-Rickardt et al., "Evidence for a Differential Avidity Model of T Cell Selection in the Thymus", <i>Cell</i> , 76:651-663 (1994)
AU4	Hogquist et al., "T Cell Receptor Antagonist Peptides Induce Positive Selection", <i>Cell</i> , 76:17-27 (1994)
AV4	Sebzda et al., "Positive and Negative Thymocyte Selection Induced by Different Concentrations of a Single Peptide", <i>Science</i> 263:1615-1618 (1994)

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AW4	Williams, "Thyroid Disease: A Case of Cell Suicide?", <i>Science</i> , 275:926 (1997)
AX4	Walker, et al., "Crystal Structure of the Cystein Protease Interleukin-1 $\beta$ -Converting Enzyme: A (p20/p10) <sub>2</sub> Homodimer", <i>Cell</i> , 78:343-352 (1994)
AY4	Wilson, et al., "Structure and Mechanism of Interleukin-1 $\beta$ Converting Enzyme", <i>Nature</i> , 370:270-275 (1994)
AZ4	Sentman, et al., "bcl-2 Inhibits Multiple Forms of Apoptosis but Not Negative Selection in Thymocytes", <i>Cell</i> , 67:879-888 (1991)
AR5	Li, et al., "Mice Deficient in IL-1 $\beta$ -Converting Enzyme Are Defective in Productin of Mature IL-1 $\beta$ and Resistant to Endotoxic Shock", <i>Cell</i> , 80:401-411 (1995)
AS5	Kuida, et al., "Altered Cytokine Export and Apoptosis in Mice Deficient in Interleukin-1 $\beta$ Converting Enzyme", <i>Science</i> , 267:2000-2003 (1995)
AT5	Rozzo, et al., "Development of the T Cell Receptor Repertoire in <i>lpr</i> Mice", <i>Sem. in Immunol.</i> , 6:19-26 (1994)
AU5	Smith, et al., "Crma Expression in T Lymphocytes of Transgenic Mice Inhibits CD95 (Fas/APO-1)-Transduced Apoptosis, but Does Not Cause Lymphadenopathy or Autoimmune Disease", <i>EMBO J.</i> , 15(19):5167-5176 (1996)
AV5	Crispe, "Fatal Interactions: Fas-Induced Apoptosis of Mature T Cells", <i>Immunity</i> , 1:347-349 (1994)

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